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## Effects of Afferent Stimulation of the Lingual Nerve on Gastrointestinal Motility in the Rat

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## Abstract

Effects of afferent stimulation of the lingual nerve (LNAS) on gastrointestinal motility and the reflex pathways which mediate the response to LNAS were investigated in rats. LNAS induced excitatory, inhibitory or biphasic responses in the stomach, duodenum and proximal colon. These responses continued after bilateral vagotomy, but were abolished after additional bilateral splanchnicotomy or transection of the spinal cord between Th4 and Th5. The inhibitory, excitatory and biphasic responses induced by LNAS were not affected by decerebration. Both after administration of atropine (0.2 mg/kg, i.v.) and guanethidine (3-5 mg/kg, i.v.), LNAS-induced excitatory and inhibitory responses were abolished in most cases, but the slight inhibitory response in the stomach and duodenum to LNAS remained in a few cases. These results suggest that the reflex centers which cause LNAS-induced excitatory and inhibitory responses are located in the dorsal nucleus of vagus and that the reflex pathways include the vagus and splanchnic nerves.

**KEYWORDS:** lingul nerve afferent stimulation (LNAS), vagus nerve, splanchnic nerve, stomach, duodenum, proximal colon, gastrointestinal motility

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## Effects of Afferent Stimulation of the Lingual Nerve on Gastrointestinal Motility in the Rat

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Effects of afferent stimulation of the lingual nerve (LNAS) on gastrointestinal motility and the reflex pathways which mediate the response to LNAS were investigated in rats. LNAS induced excitatory, inhibitory or biphasic responses in the stomach, duodenum and proximal colon. These responses continued after bilateral vagotomy, but were abolished after additional bilateral splanchnicotomy or transection of the spinal cord between Th<sub>4</sub> and Th<sub>5</sub>. The inhibitory, excitatory and biphasic responses induced by LNAS were not affected by decerebration. Both after administration of atropine (0.2 mg/kg, i.v.) and guanethidine (3-5 mg/kg, i.v.), LNAS-induced excitatory and inhibitory responses were abolished in most cases, but the slight inhibitory response in the stomach and duodenum to LNAS remained in a few cases. These results suggest that the reflex centers which cause LNAS-induced excitatory and inhibitory responses are located in the dorsal nucleus of vagus and that the reflex pathways include the vagus and splanchnic nerves.

**Key words :** lingual nerve afferent stimulation (LNAS), vagus nerve, splanchnic nerve, stomach, duodenum, proximal colon, gastrointestinal motility

It has been found that stimulation of areas innervated by the trigeminal nerve induce various effects on cardiovascular and respiratory organs (1-5). Yokota (6) reported that mechanical and electrical stimulations of the dorsum of the nose or inner mucous membrane of the nasal cavity induced evoked reflex activity in the superior and inferior lingual nerve in the cat. Kronert *et al.* (7) reported that thermal stimulation of the tongue caused vasodilation and vasoconstriction of the tongue in the dog. Kobori (8) recorded reflex activity of the vagus nerve evoked by afferent stimulation of the trigeminal nerve in the rat. Ikuno (9) reported that stimulation of the tooth pulp induced a respiratory inhibitory reflex in the cat. Nando (10) reported that the same stimulation in-

duced an inhibitory or excitatory response in gastrointestinal motility of the rabbit. However, the effect of stimulation of the tongue or lingual nerve on gastrointestinal motility has not been investigated. In the present experiment, effects of afferent stimulation of the lingual nerve (LNAS) on gastrointestinal motility and the reflex pathway were examined.

### Materials and Methods

Thirty-five rats of either sex (250-350 g) anesthetized with urethane (0.8 g/kg, i.p.) were fixed in a temperature-controlled chamber. The abdominal cavity was opened surgically, and miniature strain gauge transducers (7 mm in length, 4 mm in wide) were sewn on the serosal surface of the

stomach (1-1.5 cm oral to the pylorus), duodenum (1.5-2 cm anal to the pylorus) and proximal colon (4-5 cm anal to the ceco-colonic junction) to record the motility of these organs. After the abdominal wall was closed, recording of the motility was started using a pen oscillograph (Sanei) via a carrier amplifier (Nihon Kohden).

The lingual nerve was sectioned just proximal to where it enters the tongue, and all of its branches were severed. Afferent electrical stimulation (15-20 Hz, 0.5-0.8 msec, 2-4 V) of the lingual nerve was carried out through a platinum bipolar electrode touching the nerve in a pool of a liquid paraffin and vaseline mixture (1 : 3-4). The duration and interval of the lingual nerve afferent stimulation (LNAS) were 1 min and 15 min, respectively.

The efferent electrical activities of the gastric branch of the vagus nerve and of the preganglionic fibers of the greater splanchnic nerve, except the suprarenal nerve, were recorded with a bipolar platinum electrode. Both neural activities were fed into a pulse counter via a biophysical amplifier (time constant 0.003 sec, Nihon Kohden) and window discriminator, and their frequencies were recorded as a histogram on the pen oscillograph (Nihon Kohden).

Cannulas were inserted into the carotid artery and external jugular vein to record the blood pressure and to administer drugs, respectively.

The drugs used were atropine sulfate (Dainippon Seiyaku), guanethidine sulfate (Tokyo-kasei) and hexamethonium bromide ( $C_6$ , Sigma).

## Results

Afferent electrical stimulation of the lingual nerve induced an excitatory or an inhibitory response on the motility of the stomach, duodenum and proximal colon. Since stimulation at intervals of less than 5 min gradually reduced the magnitude of the response, the nerve was stimulated at intervals of more than 15 min. The LNAS-induced response did not reverse in character (for instance, excitation into inhibition) at any time in an experiment in one animal, even if parameters of the stimulus were altered.

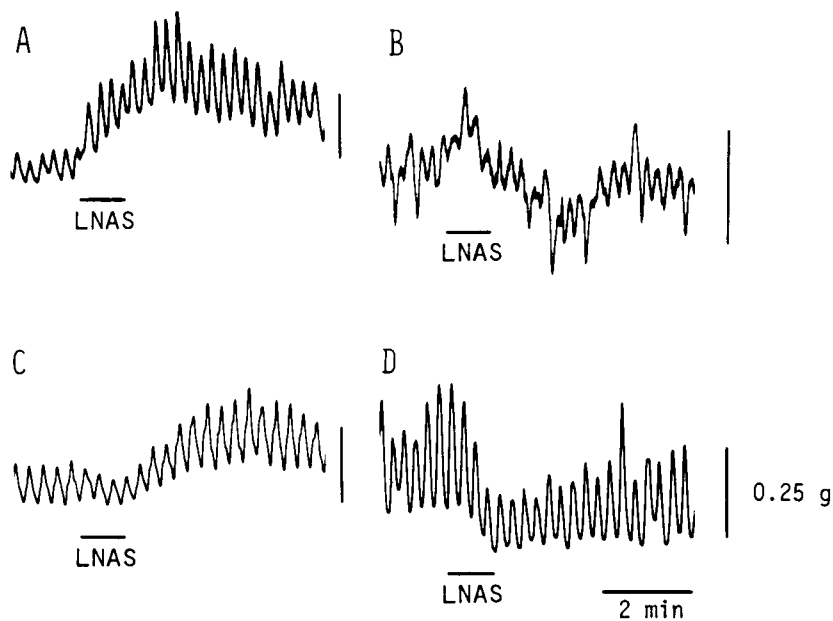
LNAS was most effective on stomach, duodenum and proximal colon at 0.5-0.8 msec, 15-20 Hz, and 2-4 V.

### *Effect of LNAS on Gastric, Duodenal and Proximal Colonic Motility*

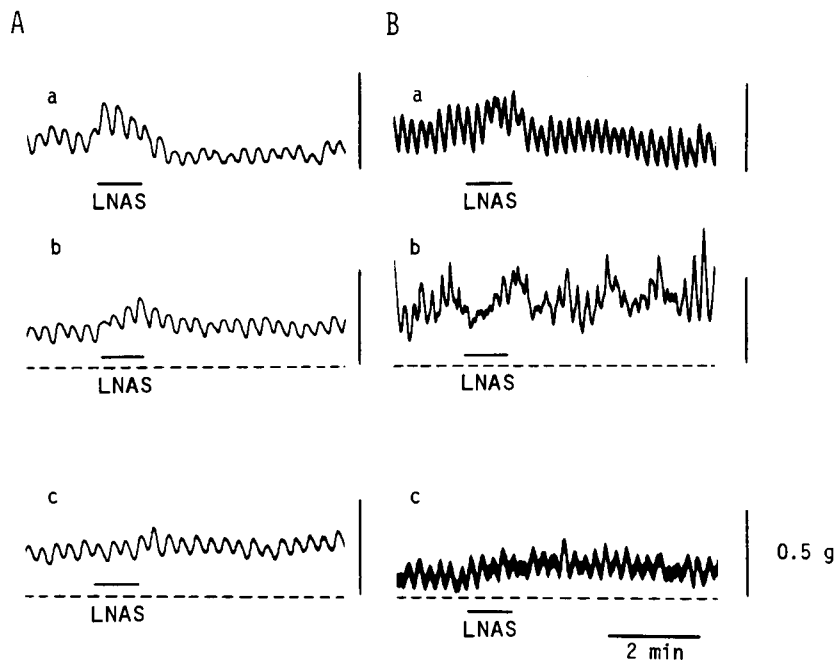
The effects of LNAS were examined on the gastric, duodenal and proximal colonic motility in 19, 19 and 16 animals, respectively. An LNAS-induced excitatory response on the stomach, duodenum and proximal colon was observed in 73.7%, 89.3% and 50.0% of the animals, respectively. The excitatory response was observed as an increase in the amplitude of phasic contractions or an elevation of the tone with (Fig. 1A) or without (Fig. 2B) an increase in the amplitude of phasic contractions. An excitatory response followed by an inhibitory one was observed on the stomach in 10.5% of the animals (Fig. 1B). An inhibitory response followed by an excitatory one after termination of the stimulation on the stomach (Fig. 1C) and duodenum was observed in 5.3% and 5.3% of the animals, respectively. An inhibitory response on the stomach (Fig. 1D), duodenum and proximal colon was observed in 10.5%, 5.3% and 18.7% of the animals, respectively. The inhibitory response was observed as a decrease in the amplitude of phasic contractions or a decline in the tone with or without a decrease in the amplitude of the phasic contractions. No response was found on the proximal colon in 31.3% of the animals. Total numbers of the LNAS-induced responses on the stomach, duodenum and proximal colon are shown in Table 1.

### *Effects of Bilateral Splanchnicotomy, Vagotomy and Transection of the Spinal Cord on LNAS-induced Response on the Stomach, Duodenum and Proximal Colon*

*Effects of bilateral splanchnicotomy followed by vagotomy.* Effects of bilateral splanchnicotomy followed by vagotomy on the LNAS-induced response on the stomach and duodenum were examined in 4 animals,



**Fig. 1** Various responses of gastric motility induced by lingual nerve afferent stimulation. A, excitatory response; B, excitatory response followed by inhibition; C, inhibitory response followed by excitation; D, inhibitory response. LNAS, lingual nerve afferent stimulation (10-20 Hz, 0.5 msec, 2-4 V). The vertical bars show 0.25 g.



**Fig. 2** Effects of bilateral splanchnicotomy and vagotomy on LNAS-induced response of the stomach. Aa, Ba, control; Ab, Bb, after bilateral splanchnicotomy; Ac, Bc, after bilateral splanchnicotomy and vagotomy. LNAS, 20 Hz, 0.5 msec and 3 V in A and 15 Hz, 0.5 msec and 3 V in B. The vertical bars show 0.5 g. The dotted lines indicate the control tone level.

**Table 1** Numbers of various responses induced by LNAS on the stomach, duodenum and proximal colon of the rats

Organs	Number examined	Number (%) showing				
		Excitation	Excitation followed by inhibition	Inhibition	Inhibition followed by excitation	No response
Stomach	19	14 (73.7%)	2 (10.5%)	2 (10.5%)	1 (5.3%)	0 (0%)
Duodenum	19	17 (89.4%)	0 (0%)	1 (5.3%)	1 (5.3%)	0 (0%)
Proximal colon	16	8 (50.0%)	0 (0%)	3 (18.7%)	0 (0%)	5 (31.3%)

and the response on the proximal colon in 3 animals.

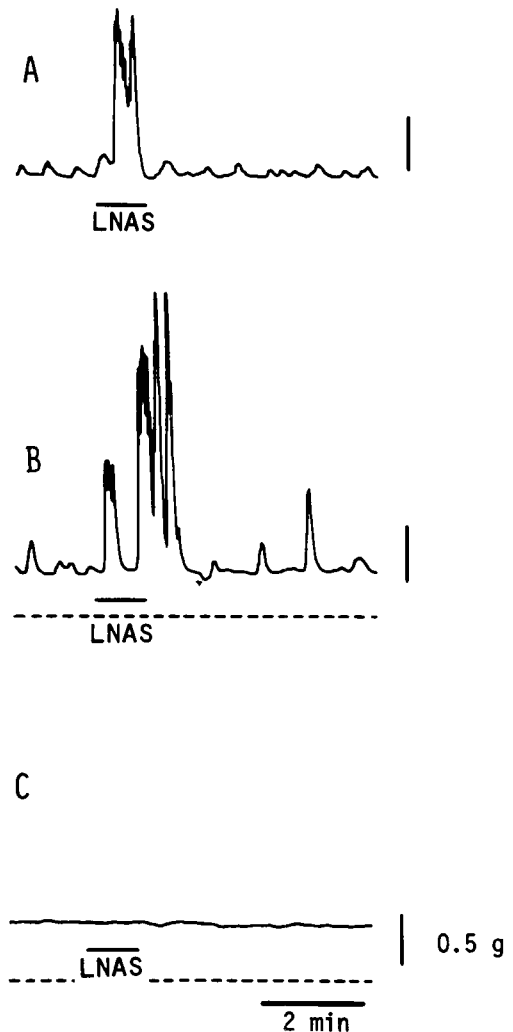
The LNAS-induced excitatory response on the stomach did not change in 2 animals after splanchnicotomy (Fig. 2Ab), while, it was reversed to an inhibitory one in one of the other 2 animals (Fig. 2Bb). In the remaining animals in which an inhibitory response was induced by LNAS on the stomach, the response was reversed to an excitatory one after splanchnicotomy.

The LNAS-induced excitatory response on the duodenum did not change after splanchnicotomy in 3 animals (Fig. 3A, B), while in one animal, it was reversed to an inhibitory response after bilateral splanchnicotomy.

LNAS caused an excitatory response of colonic motility (Fig. 4A) in 2 animals, and an inhibitory response in one animal. The LNAS-induced excitatory response was not altered by splanchnicotomy (Fig. 4B), but the inhibitory response on the proximal colon was abolished by bilateral splanchnicotomy without vagotomy.

These LNAS-induced excitatory and inhibitory responses after splanchnicotomy on the stomach, duodenum and proximal colon were abolished subsequent bilateral vagotomy in all cases (Fig. 2Ac, Bc, 3C and 4C).

*Effects of bilateral vagotomy followed by splanchnicotomy.* Effects of bilateral vagotomy followed by splanchnicotomy on the LNAS-induced response was examined in 4 animals. In one of the 4 animals, the response on the proximal colon was not exam-



**Fig. 3** Effects of bilateral splanchnicotomy and vagotomy on the LNAS-induced duodenal contraction. A, control; B, after bilateral splanchnicotomy; C, after bilateral vagotomy and splanchnicotomy. LNAS, 15 Hz, 0.5 msec and 3 V. The vertical bars show 0.5 g.

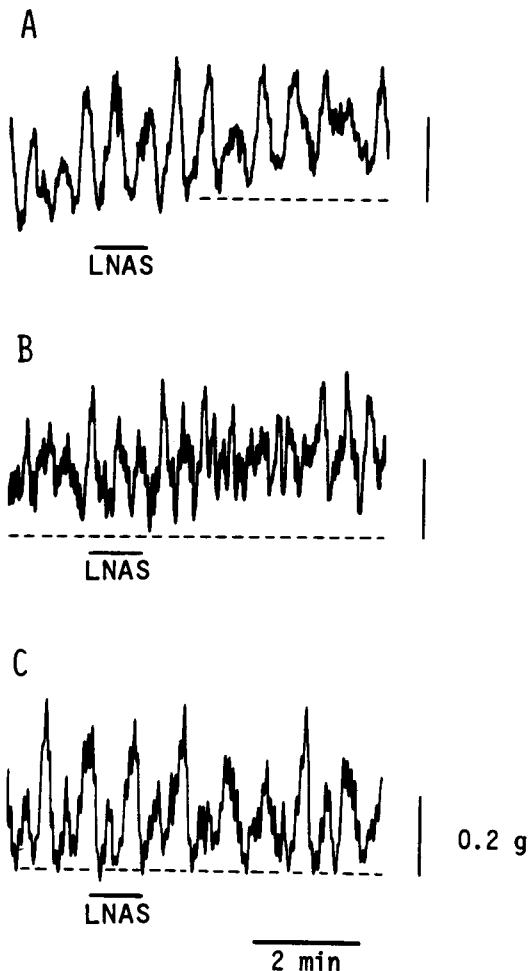


Fig. 4 Effects of bilateral splanchnicotomy and vagotomy on the LNAS-induced response of the proximal colon. A, control; B, after bilateral splanchnicotomy; C, after bilateral splanchnicotomy and vagotomy. LNAS, 15 Hz, 0.5 msec and 3 V. The vertical bars show 0.2 g.

ined.

The LNAS-induced excitatory response on the stomach was reversed to an inhibitory one by vagotomy in 3 animals. However, in the fourth animal, the LNAS-induced inhibitory response was reversed to an excitatory one.

The excitatory response on the duodenum was reversed to an inhibitory one by bilateral vagotomy in 2 animals, but in one animal, the excitatory response did not change.

In another intact animal, in which an inhibitory response was induced by LNAS, the inhibitory response was followed by an excitatory one after bilateral vagotomy.

The excitatory response to LNAS on the proximal colon was abolished by bilateral vagotomy in one animal, while the inhibitory response did not change after bilateral vagotomy in another animal. In the remaining animal, LNAS induced no response initially, but produced an inhibitory response after vagotomy.

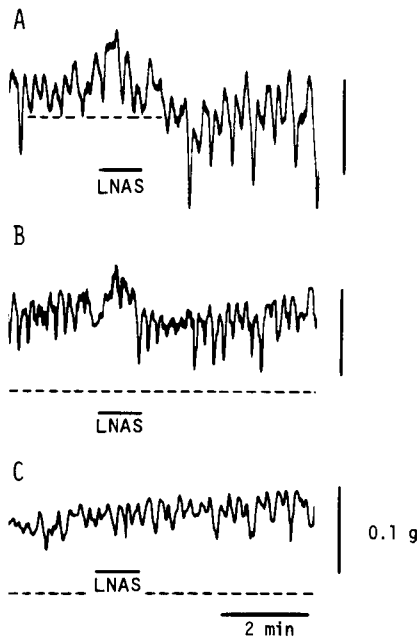
The responses on the stomach, duodenum and proximal colon which remained after vagotomy were abolished following bilateral splanchnicotomy in all cases.

A combination of bilateral vagotomy and transection of the spinal cord between Th<sub>4</sub> and Th<sub>5</sub> induced the same effect on the LNAS-induced response as a combination of bilateral vagotomy and splanchnicotomy in the stomach, duodenum and proximal colon of all animals. *Effects of Guanethidine, Atropine and C<sub>6</sub> on LNAS-Induced Responses on the Stomach, Duodenum and Proximal Colon*

Effects of guanethidine and atropine on the LNAS-induced response was examined in 7 animals. In 3 of the 7 animals, the response on the duodenum and proximal colon was not examined.

The LNAS-induced excitatory response on the stomach was not altered or increased by guanethidine administration (5 mg/kg, i.v.) in 3 animals (Fig. 5A, B). It was reversed to an inhibitory response or an inhibitory response followed by an excitatory one after guanethidine (5 mg/kg, i.v.) in 2 other animals. Additional administration of atropine (0.2 mg/kg, i.v.) abolished the remaining response (Fig. 5C). In the remaining 2 animals, the inhibitory response on the stomach after guanethidine was not abolished by atropine (0.2 mg/kg, i.v.).

The LNAS-induced excitatory response on the duodenum did not change after gua-

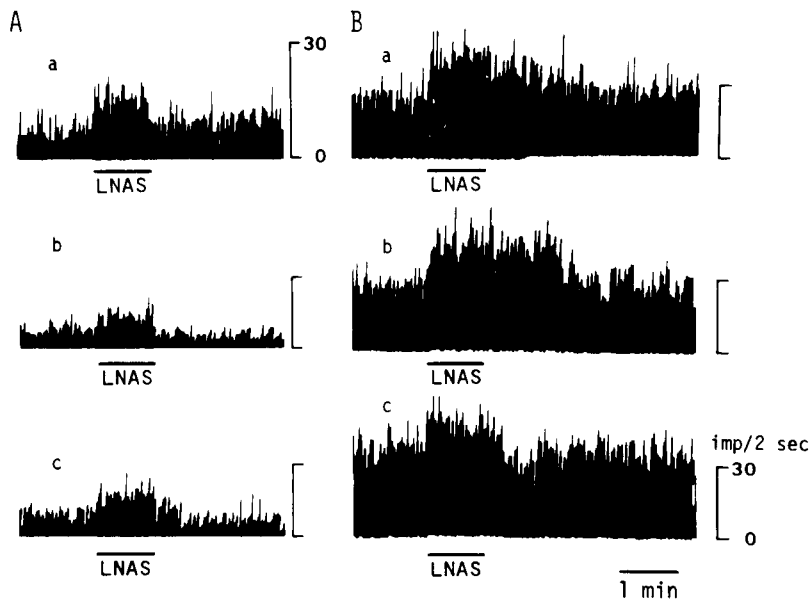


**Fig. 5** Effects of guanethidine and atropine on LNAS-induced response of the stomach. A, control; B, after guanethidine 5 mg/kg, i.v.; C, after additional administration of atropine 0.2 mg/kg, i.v. LNAS, 20 Hz, 0.5 msec and 3 V. The vertical bars show 0.1 g.

nethidine administration (5 mg/kg, i.v.) in 2 animals, but in one animal, it was reversed to an inhibitory response after guanethidine. In the remaining animal, the LNAS-induced inhibitory response on the duodenum was reversed to an excitatory one by guanethidine. An additional administration of atropine (0.2 mg/kg, i.v.) after guanethidine abolished the remaining response on the duodenum in all cases.

The LNAS-induced excitatory response of the proximal colon was reversed to an inhibitory response by guanethidine (5 mg/kg, i.v.) in 2 animals, and the inhibitory response was reversed to an excitatory response in 2 other animals. These responses which remained after guanethidine were terminated by additional administration of atropine (0.2 mg/kg, i.v.) in all cases.

$C_6$  (5 mg/kg, i.v.) reduced or abolished the excitatory and inhibitory responses on the stomach, duodenum and proximal colon in both animals examined.



**Fig. 6** Effects of lingual nerve afferent stimulation on the efferent electrical activity of the gastric branch of the vagus (A) and the splanchnic nerve efferent activity (B). a, control; b, after atropine 0.2 mg/kg, i.v.; c, after additional administration of guanethidine 5 mg/kg, i.v. LNAS, 20 Hz, 0.5 msec and 3 V. The vertical bars show the number of impulses/2 sec.



### *Effects of Decerebration on LNAS-Induced Response*

In 3 animals, the LNAS-induced inhibitory and excitatory responses of the stomach and duodenum were not affected by decerebration at a level just rostral to the superior colliculus. In one other animal, the excitatory response of the stomach and duodenum to LNAS was reduced by decerebration.

### *Effects of LNAS on Electrical Activity of the Gastric Branch of the Vagus and the Greater Splanchnic Nerves*

**Vagus nerve.** The efferent electrical activity of the gastric branch of the vagus nerve was increased about twofold (from 4.0 to 7.7 impulses/s) by LNAS ( $n = 8$ ) (Fig. 6Aa). The basal activity and this increased activity of the gastric branch did not change after atropine was administered (0.2 mg/kg, i.v.) (Fig. 6Ab), nor after additional administration of guanethidine (5 mg/kg, i.v.) in any of the animals (Fig. 6Ac).

**Greater splanchnic nerve.** The efferent electrical activity of the greater splanchnic nerve was increased about 1.5-fold (12.3 to 20.4 impulses/s) by LNAS, and this response continued over 2.5 min after termination of LNAS ( $n = 5$ ) (Fig. 6Ba, b). Atropine (0.2 mg/kg, i.v.) and guanethidine (5 mg/kg, i.v.) had no effect on the spontaneous nerve activity in any of the animals ( $n = 5$ ), but after guanethidine (5 mg/kg, i.v.), the increased activity in response to LNAS returned to the spontaneous activity level immediately after termination of LNAS (Fig. 6Bc).

### **Discussion**

In the present experiment, LNAS induced an excitatory, inhibitory or biphasic response in the stomach, duodenum and proximal colon. These responses were abolished by combining either bilateral vagotomy and bilateral splanchnicotomy or vagotomy and transection of the spinal cord.

The lingual nerve, a branch of the mandibular nerve, supplies the mucous membrane of the anterior two-thirds of the tongue and contains the special sensory fibers for taste as well as fibers sensitive to pain, touch, temperature, etc. Therefore, the excitatory, inhibitory or biphasic responses observed during afferent stimulation of the lingual nerve seem to be due to a combined effect induced by simultaneous stimulation of taste and other sensory fibers.

Kobori (8) recorded the reflex electrical activity of the cervical vagus nerve induced by afferent stimulation of the infraorbital nerve. Green (11), Foong *et al.* (12) and Tamura (5) reported that afferent stimulation of the infraorbital nerve, trigeminal nerve and tooth pulp induced evoked potentials in the trigeminal subnucleus caudalis and the dorsal nucleus of the vagus. Nando (10) reported that electrical stimulation of the rabbit tooth pulp induced either relaxation or excitation in the stomach and duodenum, and that the latter response was abolished by both bilateral vagotomy and splanchnicotomy.

In the present experiment, LNAS caused increased efferent electrical activity in the gastric branch of the vagus which induced excitation or inhibition of the gastric motility. The LNAS-induced response in the stomach, duodenum and proximal colon was reversed or depressed by vagotomy. These results indicate that LNAS, probably, influenced the activity of the vagus dorsal motor nucleus via interneurons between the trigeminal subnucleus caudalis and vagus dorsal motor nucleus, in the medulla oblongata, as many investigators have suggested (5, 6, 8-10). Nando (10) reported that gastric and duodenal excitatory or inhibitory responses to tooth pulp stimulation were abolished by splanchnicotomy after vagotomy, and that vagal and splanchnic nerve activity was facilitated simultaneously by stimulation of the tooth pulp. In the present experiment,

the LNAS-induced excitatory or inhibitory response which remained after vagotomy was abolished by splanchnicotomy or transection of the spinal cord (Th<sub>4-5</sub>). These results suggest that LNAS-induced impulses conducted to the trigeminal subnucleus caudalis descended partly from it to the spinal cord and then transmitted to the sympathetic neurons in the lateral funiculus at a level below the 4th or 5th thoracic segment.

LNAS-induced excitatory or inhibitory response on the proximal colon was abolished by vagotomy and splanchnicotomy. These results also suggest that the vagus and splanchnic nerves innervate the proximal colon. Collman *et al.* (13) noted that colonic motility was controlled by the vagus nerve in the ferret, and Harkins *et al.* (14) reported that the vagus nerve was distributed in the right half of the colon in the dog. Their reports support the present results. However, in the present experiment, no response of the proximal colon to LNAS was observed in 31.3% of the animals. This result suggests that the proximal colon in the rat probably has few innervations by the vagus and splanchnic nerves.

In the present experiment, the LNAS-induced excitatory responses in the stomach, duodenum and proximal colon were not changed or reversed to inhibitory responses by guanethidine administration or by bilateral splanchnicotomy. However, in other experiments, the excitatory response to LNAS in the stomach and duodenum was reversed to an inhibitory one after both guanethidine and atropine. These results suggest that the LNAS-induced inhibitory response in the stomach and duodenum after drug-administration or splanchnicotomy was induced by activation of the non-cholinergic non-adrenergic inhibitory neurons in the myenteric plexus via the vagus (15, 16).

Nando (10) reported that atropine reduced efferent electrical activity of the vagus

nerve evoked by tooth pulp stimulation in the rabbit and that atropine probably acted on interneurons between the trigeminal subnucleus caudalis and the vagal dorsal nucleus. In the present experiment, the spontaneous and LNAS-induced evoked electrical activity of the vagus and splanchnic nerves of the rat were not reduced by atropine and guanethidine. Therefore, it is suggested that atropine and guanethidine did not affect nervous activity in the rat brain stem. The difference in the action of atropine between the present study and that of Nando may be due to the difference in species.

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